

Statement Regarding Common Ownership

Applicants acknowledge that the claims were commonly owned at the time of the invention.

Affirmation of Election/Restriction

Applicants' affirm the election made to the Restriction Requirement on January 17, 2003. The claims of Group III (Claims 13-16 and 19) drawn to a method of treating anxiety are elected for prosecution. Applicants reserve the right to file a continuing application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicants do not hereby abandon or waive any rights in the non-elected inventions.

Rejection of Claims 13-16 and 19 Under 35 U.S.C. §103(a)

Claims 13-16 and 19 are rejected under 35 U.S.C. §103(a) as being unpatentable over Cassels *et al.* (USPN 5,756,538) ("Cassels"). According to the Examiner,

Cassels *et al* teaches a method of treating anxiety comprising administering to the patient an effective non-toxic amount of substituted flavonoid, particularly substituted flavone, wherein the substituents may be hydroxyl group or low alkyl alkoxyl groups.

The Examiner goes on to state that although Cassels does not teach expressly the employment of the flavone therein with R4 being a methoxyl group, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to treat anxiety by employing a flavone with hydroxyl groups at positions 5 and 7, and a methoxyl group at position 8 (R4 as depicted by Cassels). Applicants respectfully disagree.

Cassels describes a method of treating anxiety comprising administering to the patient a substituted flavonoid of the general formula (I). All the possible substituents that can be selected for each of the positions in general formula I are listed (see Cassels col. 1, lines 58-63) as well as a list of the preferred substituents (see Cassels col. 3, lines 16-36). By selecting the proper substituents for the proper positions, one could create a compound having hydroxyl groups at positions R1 and R3 (positions 5 and 7 of the instant application) and a methoxyl group at R4 (position 8 in the instant application). However, Cassels does not explicitly teach this

combination of substituents and none of the working examples use a substituted flavone having this combination of substituents.

The selection of substituents by Applicants is not trivial as demonstrated by comparing Figure 3 of the instant application with Figure 2 of Cassels. The claimed compound displays significant anxiolytic effects in mice at dosages of 7.5, 15 and/or 30 mg/kg. Note that a dosage range of about 7.5 mg/kg to about 30 mg/kg in mice is the equivalent to a dosage range of about 0.8 mg/kg to about 3.3 mg/kg in humans, which is a therapeutic dose range in humans.

According to Figure 2 of Cassels, the optimal dose in mice of the compounds described in Cassels is 1 mg/kg and the anxiolytic properties of these compounds diminishes greatly as the dosage levels are increased. In fact, a dose of 10 mg/kg of the Cassels compound provided less anxiolytic effect than the "delivery vehicle alone" control. Thus, Cassels teaches away from preparing a substituted flavonoid having the anxiolytic dosage properties achieved by Applicants.

Cassels neither teaches the claimed selection of substituents nor suggests that the claimed selection would significantly improve the anxiolytic properties of the substituted flavonoid. As such, one of skill in the art, at the time of the invention, would not have been motivated by the teachings of Cassels to make a compound having the claimed selection of substituents with a reasonable expectation of success of providing a substituted flavonoid for the treatment of anxiety having anxiolytic properties over a dosage range that is therapeutically effective in humans. Thus, Claims 13-16 and 19 are non-obvious over the cited reference. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,  
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